Country-level cost-effectiveness thresholds: initial estimates and the need for further research

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Financial support: This research report was produced as part of the Lablite project (http://www.lablite.org/), as well as the International Decision Support Initiative (www.idsihealth.org), a global initiative to support decision makers in priority-setting for universal health coverage. This work received funding support from the Bill & Melinda Gates Foundation, the Department for International Development (UK), and the Rockefeller Foundation. Mark Sculpher receives support from the UK National Institute for Health Research as a Senior Investigator (NF-SI-0513-10060). The views expressed are those of the authors and not necessarily those of the funders.

Key words: Threshold; Cost-effectiveness; Willingness to pay; Quality Adjusted Life Years; Benefits package; Universal Health Care.

Running title: Country-level cost effectiveness thresholds

Acknowledgements: We thank attendees at the Health Economics Study Group in Leeds, January 2015 for useful feedback on an earlier draft of this manuscript.

Abstract (max 250)

Objectives: Cost-effectiveness analysis (CEA) can guide policymakers in resource allocation decisions. CEA assesses whether the health gains offered by an intervention are large enough relative to any additional costs to warrant adoption. Where there are constraints on the healthcare system's budget or ability to increase expenditures, additional costs imposed by interventions have an 'opportunity cost' in terms of the health foregone as other interventions cannot be provided. Cost-effectiveness thresholds (CETs) are typically used to assess whether an intervention is worthwhile and should reflect health opportunity cost. However, CETs used by some decision makers - such as the World Health Organization (WHO) suggested CETs of 1-3 times gross domestic product per capita (GDP pc) - do not. This study estimates CETs based on opportunity cost for a wide range of countries.

Methods: We estimate CETs based upon recent empirical estimates of opportunity cost (from the English NHS), estimates of the relationship between country GDP pc and the value of a statistical life, and a series of explicit assumptions.

Results: CETs for Malawi (the lowest income country in the world), Cambodia (borderline low/low-middle income), El Salvador (borderline low-middle/upper-middle) and Kazakhstan (borderline high-middle/high) are estimated to be $3-116 (1-51% GDP pc), $44-518 (4-51%), $422-1,967 (11-51%) and $4,485-8,018 (32-59%); respectively.

Conclusions: To date opportunity cost-based CETs for low/middle income countries have not been available. Although uncertainty exists in the underlying assumptions, these estimates can provide a useful input to inform resource allocation decisions and suggest that routinely used CETs have been too high.

Introduction

Policy-makers in all healthcare systems face difficult choices about which interventions, programmes or activities (hereinafter referred to solely as 'interventions') should be funded from limited available resources. The tools of economic evaluation offer a variety of means to assist policymakers in the process of prioritisation. A common approach is incremental cost-effectiveness analysis (CEA) which is based upon the comparative assessment of costs and benefits, with the latter generally focussed on health gains. CEA seeks to identify which interventions offer health gains large enough, relative to their costs, to warrant adoption.[1]

CEA typically includes detailed information about the incremental costs ($\Delta\, costs$) and incremental health effects ($\Delta\, health$) of an intervention relative to alternative interventions. The results of CEA are often expressed as an incremental cost-effectiveness ratio (ICER); the ratio of incremental costs to incremental health effects ($^{\Delta\, costs}/_{\Delta\, health}$).[1] Health effects are often represented as quality adjusted life years (QALYs) or disability adjusted life years (DALYs) averted; and so the ICER gives the 'cost per QALY-gained/DALY-averted' associated with an intervention. Although these are useful summaries, the question remains as to whether a particular cost per QALY-gained/DALY-averted ought to lead to the evaluated intervention being considered cost-effective.

If an intervention offers incremental health gains but at some additional costs then a decision regarding whether it should be funded should be informed by the value of what will be given up as a consequence of those costs (i.e. the opportunity cost of funding the intervention[2]). All systems face some restrictions on the resources available for healthcare. If resources are committed to the funding of one intervention then they are not available to fund and deliver others. The opportunity cost of a commitment of resources is, therefore, the health forgone as these "other" interventions that are available to the health system cannot be delivered. Even if additional resources are placed into the healthcare system to be made available for a particular new intervention, there is an opportunity cost to these resources - the health that could have been gained by investing these additional resources elsewhere in the system.

In the context of CEA, the opportunity cost can be expressed using a cost-effectiveness threshold (CET). CETs based on opportunity costs describe the amount of money that, if removed from the healthcare system, would result in one less unit of health being generated, or equivalently, the cost of generating health in the current system. In the case of the introduction of a new intervention that imposes additional costs on the system, this is equivalent to a marginal reduction in the resources available for other activities. If the ICER (cost per QALY/DALY gained) is less than the CET it means that diverting funds to the intervention will increase population health. For example if the CET is $1000/QALY and the ICER for an intervention is $100/QALY, then for every $1000 spent on the intervention 1 QALY is lost in the wider healthcare system but 10 are gained from the new intervention. The net health effect is positive. Therefore, if an ICER<CET, an intervention can be considered 'cost-effective'; but if ICER>CET the benefits are insufficient in comparison to costs and the intervention can be considered not to be cost-effective. Hence CEA simplifies to an assessment of whether a new intervention will result in gains in population health and the inverse of the CET should reflect the marginal product of healthcare spending ($^{\Delta\, health}/_{\Delta\, costs}$).

Estimating the opportunity cost of healthcare spending (estimating the CET) is, therefore, a crucial aspect of any resource allocation decision in healthcare.

Understanding cost-effectiveness thresholds

Recent methods research has emphasised the centrality of opportunity costs in informing resource allocation decisions and how CETs can be appropriately estimated for CEA to inform decisions aimed at improving population health[3, 4] – see Drummond et al. (2015) chapter 4 for a full overview.[1] A clear distinction needs to be made between two related, but separate, concepts which have informed the debate regarding the most appropriate value for the CET: (i) opportunity costs in terms of health foregone when costs fall on healthcare budgets; and (ii) opportunity costs in terms of foregone consumption (the 'consumption value of health') when additional costs fall on consumption opportunities outside healthcare. The first is an issue of ‘fact’, resulting from limits in the overall collective budget available for healthcare or constraints on health system’s abilities to increase expenditure. It reflects the health currently generated from the healthcare system (or that could be gained if expenditure were increased) and, therefore, reflects the “supply side” of the system. The second is an issue of ‘value’ and depends upon how individuals and society value health as compared to other forms of consumption or non-health publicly funded goods. This indicates what individuals and society want from the healthcare system; or the “demand side”.

For economic evaluation it is important to consider what type of opportunity costs would result from investment in new activities. If opportunity costs result in the form of health forgone (e.g. through displacement of other health generating interventions), then the CET should reflect this – let’s denote this ‘*k*’ (the amount of money that would displace one QALY’s worth of healthcare investment). If opportunity costs are in terms of other forms of consumption, the CET should reflect the consumption value of health - let’s denote this ‘*v*’.

If we observe that the consumption value of health is higher than the amount of healthcare resource required to improve health ($v > k$) then this suggests that the healthcare system is not meeting individual preferences. Individuals would be willing to give up more of the resources available to them to improve their own health than the healthcare system would require. There are a number of reasons why this may be the case, not least the welfare losses associated with socially acceptable ways to finance healthcare systems and the fact that individuals may be willing to expend more resources improving their own health than improving the health of others via a collectively funded system.

For incremental CEA to inform the allocation of healthcare expenditures, for which the primarily purpose is generally regarded as being the generation of health from limited collective healthcare resources, CETs reflecting the opportunity costs of healthcare spending (*k*) will always be required if there are any restrictions on the growth in healthcare expenditure (see Drummond et al (2015) chapter 4, section 4.3.4).[1]

Estimating cost-effectiveness thresholds

CETs have not generally been set to reflect *k*. For instance, values of GB£20-30,000 andUS$50,000 have commonly been applied in the United Kingdom and United States, respectively.[5, 6] Similarly, for low and middle income countries, the World Health Organization (WHO) has recommended thresholds of 1 to 3 times gross domestic product per capita (GDP pc).[7] These values are not based upon assessment of health opportunity costs resulting from resource constraints. The basis for these thresholds is unclear; however, they appear to have been conceptually and to some degree empirically informed by the consumption value of health (or more accurately estimates of individuals willingness to pay (WTP) to improve their own health) – for instance, the WHO threshold is described as being based on estimates reported in the "Commission on Macroeconomics and Health" report from 2001.[8] These estimates were intended to inform decisions regarding overall investments in healthcare spending and used estimates of the WTP for mortality risk reductions. Indeed, similar approaches continue to be used to advocate for increased healthcare spending.[9] However, the use of these thresholds when assessing the value of individual interventions in the context of existing spending limits is not consistent with population health improvement, as they do not reflect the opportunity costs that are imposed on healthcare systems. Although demand side thresholds might inform social choices about the magnitude of financial resources committed to healthcare, they are inappropriate measures of health opportunity cost and so risk reducing, rather than increasing, population health when used in the context of CEA.

Alternatively, the relationship between changes in healthcare expenditure and health outcomes - the marginal productivity of the healthcare system in generating health - can be estimated. This provides a direct measure of the health consequence of changes in available resources, e.g., when a cost-escalating intervention is adopted or what could be gained if additional resources are made available in general to fund healthcare. Using such estimates of *k* to inform CETs provides a basis for informing resource allocation decisions with a view to increasing population health. However, there is a paucity of estimates of CETs using these approaches. One notable exception is Claxton et al.[4] who used local level programme expenditure data, in a range of disease areas, to estimate the relationship between changes in healthcare expenditure and health outcomes in the English National Health Service (see Drummond et al (2015), chapter 4, for a full description of this work).[1]

By exploiting the variation in expenditure and in mortality outcomes, Claxton et al. estimate the relationship between changes in spending and mortality in those clinical programme areas in which a mortality effect could be identified, while accounting for endogeneity. With additional information about age and gender of the patient population, these mortality effects were expressed as a cost per life year threshold (£25,241 per life year). These life year effects were adjusted for quality of life using additional information about quality of life norms by age and gender, as well as the quality of life impacts of different types of disease. By using the effect of expenditure on the mortality and life year burden of disease as a surrogate for the effects on a more complete measure of health burden (i.e. that includes quality of life burden) a cost per QALY threshold was estimated. This was subject to parameter and structural uncertainty, but a central estimate of UK £12,936 per QALY was reported.[4]

There is growing recognition of the need for estimates of *k* that reflect opportunity costs in terms of health to inform resource allocation decisions in low, middle and high income countries.[10, 11] However, with the exception of the work by Claxton et al., there is a lack of empirically based estimates of *k*. This paper draws out the implications of what the limited available evidence suggests about 'supply side' CETs (*k*'s) in a range of jurisdictions. We return to the subject of how these estimates might be used to inform resource allocation decisions in the Discussion.

Methods

The Claxton et al. estimate of *k* is based upon estimates of the marginal productivity of healthcare spending in just one jurisdiction.[4] In principle, a similar approach could be adopted to estimate the relationship between healthcare spending and health outcomes internationally, using countries as units of analysis, to determine *k* in a wide range of settings.

To date, however, cross-country evidence on the productivity of healthcare spending has focused on answering the question "does healthcare spending improve health outcomes?". Recent research adjusting for potential reverse causality in this relationship (e.g. governments may spend more when health outcomes are worse) suggests that the answer to this question is yes.[12] However, the available literature does not focus on how the effect of healthcare spending on health outcomes varies according to the level of healthcare spending or country income. The available analyses do suggest that the marginal productivity of healthcare spending diminishes with increasing healthcare spending or country income.[13-15] This indicates that the threshold should increase with country income or healthcare spending and reflects our expectation that the amount of health displaced by new resource commitments decreases as country income or healthcare spending rises. However, there is little information to quantify how the marginal productivity of healthcare spending varies with country income.

However, there is a body of literature that estimates v (the consumption value of health or 'demand-side' threshold) in different countries. Some of this literature is based upon stated preference elicitation of individuals' WTP for morbidity adjusted life years (e.g. QALYs)[16, 17], but a larger body of work estimates the 'value of a statistical life' (VSL) by estimating individuals' WTP for mortality reductions (e.g. by estimating wage compensation for on the job risk exposure).[18, 19] Moreover, this literature also examines how the VSL varies across jurisdictions as a function of national per capita income (i.e. the elasticity of the VSL with respect to income, ε). This potentially provides information about the income elasticity of v if we can assume that the income elasticity of the VSL is equal to the income elasticity of the value of a life year, and this in turn is equal to the income elasticity of the value of a morbidity adjusted life year (e.g. QALY). For this to be the case across countries, a VSL must convert to the same number of QALYs across countries (this assumption is examined in the Discussion).

Understanding the income elasticity of v across countries raises an interesting prospect. If a similar income elasticity of k exists as for v, income elastisticies of the VSL can be applied to the Claxton et al. estimate of k for the English NHS to provide estimates of k in a wide range of jurisdictions. For the income elasticity of k to equal that of v requires that the ratio between k

and *v* is constant across countries (this assumption is examined in the Discussion). We follow this approach to provide estimates of *k* for application in different countries based upon: their per capita income levels, the cost-effectiveness threshold for the UK NHS, per capita income in the UK and the elasticity of VSL with respect to income. This approach is illustrated in Figure 1 and requires the following three assumptions: (1) that the relative discrepancy between *v* and *k* is constant across countries; (2) that the values used for *k* and ε are appropriate estimates; and (3) that the income elasticity of *the value of a statistical life* (VSL) equals the income elasticity of the *consumption value of a QALY*.

The potential for these assumptions to be violated is examined in the Discussion. However, we note that the broad expectation that both *v* and *k* will increase with country income is uncontentious. As income increases basic consumption needs are met and individuals become more willing to exchange income for health (*v*) and healthcare spending expands accordingly. As income and healthcare expenditure rise, the marginal productivity of healthcare spending diminishes (*k* increases).

Our model requires that healthcare spending will increase such that the predicted increase in *k* is observed. However, we make no assumptions regarding how the expansion to healthcare is funded. It could be funded via an expansion to the tax base, a redistribution of the tax base or a combination of the two.

[Insert Figure 1 here]

The best available estimate of the UK CET is £12,936 per QALY (US$18,609 purchasing power parity (PPP) adjusted [20]). Gross domestic product (GDP) per capita estimates for 2013 were obtained from the World Bank dataset. In line with the literature on the value of a statistical life, elasticities are applied to countries' GDP per capita adjusted for purchasing power parity [21] (see for example Milligan (2014)).[22] CETs are reported in 2013 PPP adjusted US dollar values. Values without PPP adjustment are also provided alongside non-PPP adjusted GDP. [23] We use data on the ratio of the PPP conversion factor to the market exchange rate to remove the PPP adjustment but retain the presentation in dollars.[24]

Estimates of income elasticity for demand for health

The relationship between the value of a statistical life (VSL) and per capita income at the level of jurisdictions is investigated in a small but emerging literature.[19, 22, 25] The literature has evolved out of a longer standing body of work which has examined the relationship between income and health valuation at the level of individuals (i.e. 'within' countries).[18, 25] Of central interest in both these bodies of work (within-group, at the individual level, and between-group, at the level of jurisdictions) is the income elasticity of the value of health..

Initial empirical research conducted primarily in higher income countries amongst individuals, and most often in the United States, suggested elasticities in the range 0.4-0.6.[18, 19] These estimates came mainly from cross-sectional studies looking at wage-risk premiums. However, the estimates have been described as "nonsensical" when extrapolated to lower income countries since the corresponding VSL would be beyond the ranges considered plausible.[19]

The methods to estimate the income elasticities of VSL have, therefore, been more carefully scrutinized in more recent years. In particular, cross sectional ('within group') estimates from earlier studies have been contrasted with longitudinal or cohort ('between group') studies (which typically estimate elasticities>1; even within countries) and reasons for inconsistencies explored.[19, 25, 26] For instance, Aldy and Smyth (2014) use a life-cycle model applied to US data on the consumption and labour supply choices faced by individuals with uncertain life expectancy and wage income to explain this discrepancy.[26] They argue that cross-sectional studies are more likely to capture changes in realised income, whereas longitudinal or across cohort studies capture the impact of permanent income (i.e. reflecting lifetime opportunities to generate income) which is more informative when translating VSL estimates across countries. Estimates of elasticity with respect to realised income are lower as realised income is more variable.

The recent consensus then is that the income elasticity of VSL to transfer estimates across countries should be >1.[19, 22] A range of elasticities were selected for this analysis (1.0, 1.5 and 2.0) to reflect uncertainty in the literature. Based upon Milligan et al (2014), a function is also applied of an elasticity of 0.7 for 'high income' countries (those with gross domestic product (GDP) per capita >$10,725, 2005 price year, purchasing power parity), and of 2.5 for countries with per capita incomes below this threshold.[22] In line with the recommendations in Milligan et al. 2014, the elasticities from this study are applied to 2013 PPP-adjusted GDP, deflated to reflect 2005 international dollars. The resulting threshold values are then inflated to reflect 2013 international dollars.

Results

Predicted CETs across country income levels are shown in Figure 2 for a range of income elasticities for the VSL. Higher income elasticities imply lower CETs in countries with lower GDP pc compared to the UK, and higher CETs in countries with higher GDP pc compared to the UK. The impact of alternative choices of elasticity is larger as the discrepancy between the GDP of the country of interest and UK GDP widens. Results for a selection of specific countries are shown in Table 1.

[Insert Figure 2 here]

[Insert Table 1 here]

US dollar CET values with and without PPP adjustment are provided in the appendix for all countries for which data were available from the World Bank database for 2013. Values without adjustment for PPP can be converted to local currency using standard exchange rates.

As exemplar countries, for Malawi (the lowest per capita income country in the world), Cambodia (borderline low and low-middle income), El Salvador (borderline low-middle and upper-middle income) and Kazakhstan (borderline high-middle and high income) CETs are estimated to be $3-116 (1-51% GDP pc), $44-518 (4-51% GDP pc), $422-1967 (11-51% GDP pc) and $4,485-8,018 (33-59% GDP pc); respectively. For Luxembourg (the highest per capita income country in the world), we estimate a CET of $43,092-143,342 (39-129% GDP pc).

Discussion

Policymakers in all countries, whether classified as high, middle or low income, face difficult decisions about how to allocate scarce healthcare resources. CEA offers a means by which to compare the costs and health gains from interventions as a basis to inform investment decisions. For the results of CEA to align with population health improvement, health gains from recommended interventions must exceed the health foregone when resources are committed to those interventions. CETs should therefore reflect our best estimates of the opportunity cost of healthcare spending (k) and not the consumption value of health (v).

In this paper we provide indicative estimates of cost-effectiveness thresholds based on opportunity costs (the 'k's) in a number of countries that intend to reflect the likely marginal productivity of their healthcare systems. Due to the lack of attention paid to estimating k in the literature to date, the estimates are based on limited data and strong, uncertain assumptions. The estimated CETs are substantially lower than those currently used by decision-making agencies and international organizations. Compared to a threshold of US$50,000 per QALY that has been conventionally applied in the US[5] our approach estimates a CET in the range US$24,283-US$40,112 per QALY. Even more starkly, the thresholds we estimate are far below those of 1-3 times GDP pc suggested by the WHO for use in low and middle income countries.[7, 8] In the lowest income country in the world, Malawi, we estimate a CET of $3-116 (1-51% GDP pc); and in Kazakhstan, a country on the borderline between being middle and high-income, we estimate a CET of $4,485-8,018 (33-59% GDP pc). This implies that resource allocation decisions based upon WHO thresholds are likely to be recommending interventions which can lead to reductions in population health.

A separate question is how the estimates of *k* should be used by healthcare decision makers. It is argued here that understanding the full net health effects of an intervention is essential. Decision makers must understand the magnitude of direct health gains from an intervention but also the health that is expected to be displaced by the interventions costs. An understanding of what the health effects of increasing or reducing health expenditure are likely to be (a supply side threshold, *k*) is therefore necessary if social and political choices regarding resource allocation are to be made in an informed and accountable way. It is clear, therefore, that in estimating the full net health effects of an intervention only those costs that fall on the healthcare budget should be included. This approach should never, however, be considered as a single decision making rule, and instead should be an input in to a wider decision which is likely to include a range of additional considerations including important social value judgements and appropriate consideration of the effects decisions are likely to have outside of health (e.g. impact on financial protection). However, understanding the opportunity cost on health of using these additional considerations is important to guide decisions. Indeed, in the context of a financially constrained healthcare system, any widening of the measure of benefit that informs decisions should also be reflected in terms of opportunity costs (e.g. to what extent will the financial protection benefits of alternative interventions be foregone).

Estimates of the consumption value of health (*v*) have no role in decisions regarding the allocation of the scarce available resources for delivering healthcare.[1] Estimates of the consumption value of health may have a role in informing the social choice of what level of resources should be devoted to healthcare. However, estimates of individuals' willingness to trade off personal consumption for the collective health gains of increased healthcare spending might be more useful for this. It is not clear that any study to date has estimated this quantity.

The results presented rely upon some core assumptions if they are to provide reasonable estimates of the marginal productivity of other (non-UK) healthcare systems. The plausibility of each assumption is considered in turn.

(1) that the discrepancy between the consumption value of health (*v*) and cost-effectiveness threshold for health (*k*) is constant in relative terms across countries

It is assumed that the proportionate 'underfunding' of healthcare, through collectively pooled resources relative to individual preferences over consumption and health, is constant across countries.

The ratio between *k* and *v* is in fact likely to differ across country income levels. The most obvious reason for this is that healthcare budgets may differ across countries for reasons other than differences in valuations of health. In lower income countries the size of the healthcare budget is likely to be constrained by the ability of countries to raise tax revenues. The difficulties faced by low income countries in raising tax are well documented and include the presence of a large informal sector, the impact of aid on the size of the state, poor checks and balances that reduce the likelihood of common-interest spending, interest groups reducing the propensity to tax, low support for higher taxation due to perceptions of corruption and the availability of institutions to facilitate tax collection.[27] This is likely to create a downward pressure on the healthcare budget (not reflected in our analysis) that will cause *k* to be lower than we predict. As well as having implications for *k* the reduced size of the healthcare system may result in a greater demand for private healthcare spending. There may also be constraints on the ability of countries to allocate the available tax base to health as oppose to other state-funded programmes.

In lower income countries, and particularly for the poorest countries, donor funding may represent a significant component of healthcare spending. The available evidence supports some substitution of donor funding for government health spending, although the substitution is partial.[28] The net effect of donor funding is, therefore, expected to increase public healthcare spending and therefore raise *k*.

Depending on whether the restrictions on healthcare expenditure and the influx of donor funding increase or decrease the budget beyond what it would otherwise be, *k* may be smaller or larger than predicted by this analysis.

(2) that the UK estimate of *k* is correct and that the range of income elasticities (1-2) explored includes the correct value

A recent systematic review[29] identified additional studies estimating the impact of health expenditure on health outcomes. Two of these studies were by Martin et al and were precursors to the Claxton et al work.[30, 31] Lichtenberg [32] develops a production function for mortality reductions using US data. In this model health is generated by previous years of healthcare expenditures and the stock of medical innovations. However, the methods used do not allow us to disentangle the impact of time trends in expenditure from other temporal influences on health and, therefore, are unlikely to provide a robust estimate of *k*.

The UK estimate of *k* is firmly founded on empirical estimation of the effect of changes in expenditure on mortality outcomes while accounting for endogeneity. The assumptions and judgement required are summarised in Table 32 of Claxton et al 2015[33], which also provides links to text and footnotes where the qualitative effect of these assumptions are examined in greater detail. The analysis made use of the best available existing evidence and, if anything, is more likely to be conservative than optimistic with respect to the health effects of changes in NHS expenditure, i.e., is more likely to have over rather than underestimated the UK threshold.[34]

A range of values for the elasticity of the value of a statistical life (ε) was considered, informed by the literature; however, it should be noted that there is little robust data on what value ε should take. Furthermore, expressions of willingness to pay for individual health gains may differ markedly from individuals' willingness to trade consumption for collective health gains, further increasing the uncertainty around the estimates used.

(3) that the income elasticity of WTP for a QALY can be approximated by ε

For the income elasticity of the VSL to equal the income elasticity of WTP for a QALY, a statistical life saved should provide the same units of morbidity-adjusted health (e.g. QALYs) across countries. This could be questioned if lives-saved were expected to generate very different remaining morbidity-adjusted life expectancies. Although life expectancy at birth varies considerably across countries, remaining life expectancy differs much less due to differences in age demographics. For example, Hammitt and Robinson, 2011, find remaining life expectancies of between 34 and 45 years in countries with widely varying per capita incomes.[19] This is a result of much older populations in countries with higher life expectancies at birth. Although quality of life is likely to increase with income, older populations would also be expected to have higher levels of morbidity, so differences in QALYs gained may also be small.

Therefore, although our results are embedded with many assumptions, it is not immediately clear whether these are likely to lead to our estimates of *k* being positively or negatively biased.

These results should, however, only be regarded as a first attempt to inform this area of crucial policy importance. Further empirical evidence is required to inform decision makers' understanding of *k*.

Although correlations between healthcare expenditure and health are well established estimates of the *causal* effect of expenditure on health are few. Analysis of cross-country data could be used to inform international estimates of the marginal productivity of healthcare spending, and to estimate the income elasticity of *k* and estimate *k* for different countries reflecting their demographics, epidemiology, health expenditure, income and other covariates.[35]

Within-country research could take a number of forms. Where data are available, the analysis of Claxton et al. could be repeated. Econometric analyses of policy reforms and other natural experiments could also inform estimates of the marginal productivity of health spending. Another approach could be to explore the cost-effectiveness of interventions currently provided within a country and those falling outside of the budget envelope. In this way, policymakers can undergo a process of "threshold seeking"[36] and become more informed about *k* as the number of CEAs in their jurisdiction increases. One example of a study using an approach similar to this is from Malawi and suggests a threshold of no more (and perhaps less) than US$150 in that country,[37] which is slightly above the range (US$3-US$116) estimated here. Countries could also examine specific disinvestment opportunities in order to understand the health likely to be displaced by new investments. Similarly, where spending is made up of a relatively small number of interventions, a mathematical programming approach may be feasible[38, 39] This approach identifies the optimal set of interventions to adopt from a given budget. The ICER of the least cost-effective funded intervention provides an estimate of the CET.

Most importantly, any research intended to inform CETs should focus on estimating the opportunity cost of healthcare spending i.e. should focus on *k* not *v*. As more empirical evidence emerges for specific countries there may also be value in synthesising this information to provide better informed extrapolations across countries.

Conclusion

To date there have been no estimates of opportunity cost-based CETs (*k*'s) for low or middle-income countries. This paper draws out the implications of the limited available evidence to estimate opportunity-cost based CETs for a range of countries. The overall conclusion is that the balance of evidence suggests that CETs used to date – such as the WHO estimates – are too high and should not be used to inform resource allocation decisions. Further research is needed to inform this key but neglected question. In the meantime, decision makers may want to use estimates generated here alongside country-specific information on the opportunity cost of healthcare funds to inform their resource allocation decisions.

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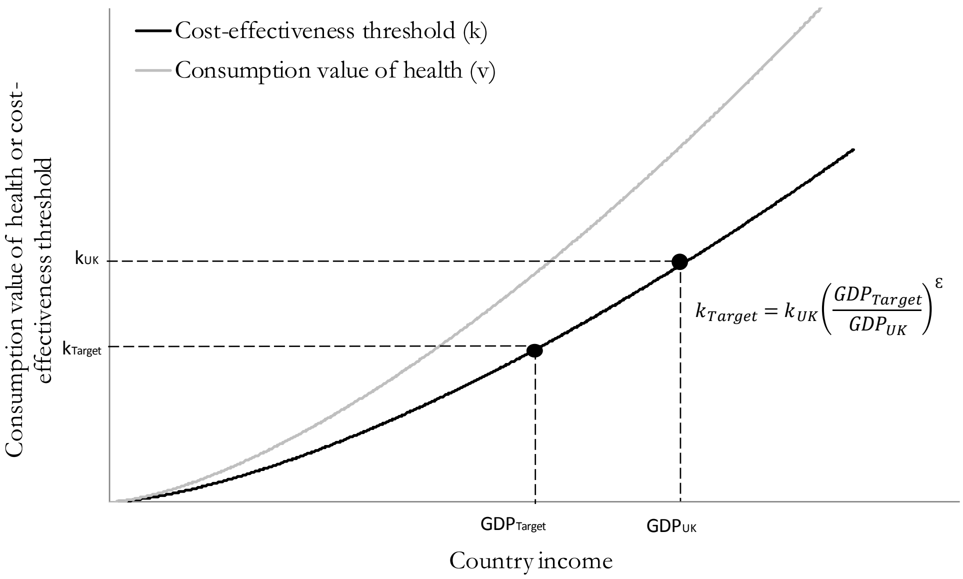

Figure 1: Method for inferring country-specific cost-effectiveness thresholds from UK threshold

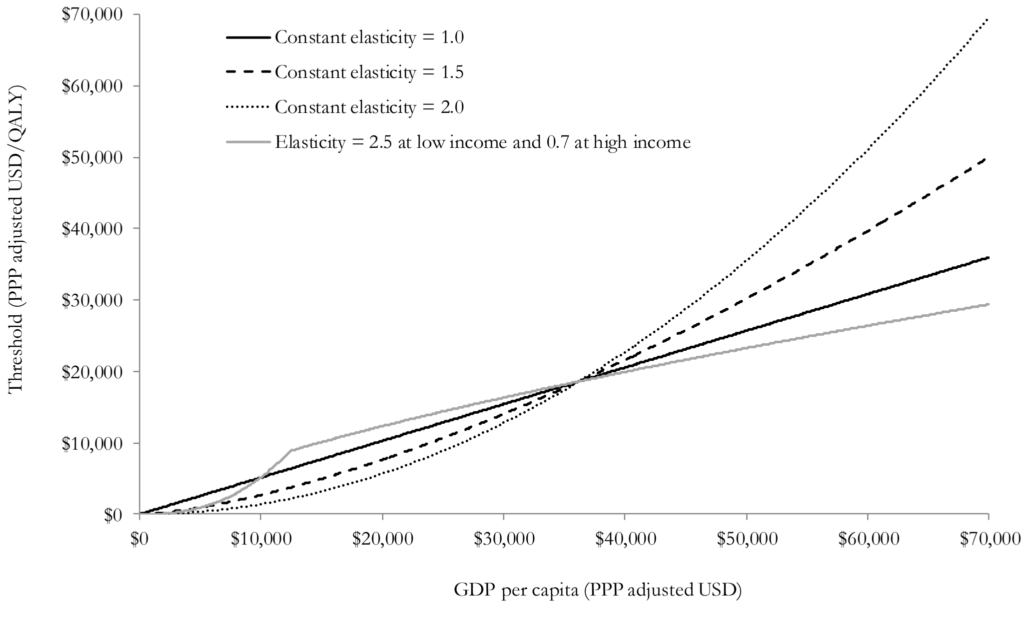

Figure 2: Predicted cost-effectiveness threshold (k) values by country income

Table 1: Example results for a range of countries and the World Bank income classification cut-offs (2013 GDP per capita)

	PPP-adjusted (2013 USD)		Actual values (2013 USD)		Threshold as % GDP p.c.
Country/classification	GDP p.c.	Threshold range+	GDP p.c.	Threshold range+	
Malawi	780	9 - 401	226	3 - 116	1% - 51%
Indonesia	9,559	1,298 - 4,914	3,475	472 - 1,786	14% - 51%
Chile	21,911	6,819 - 13,141	15,732	4,896 - 9,436	31% - 60%
Kazakhstan	23,206	7,648 - 13,675	13,610	4,485 - 8,018	33% - 59%
United kingdom	36,197	18,609 - 18,609	41,787	20,223 - 20,223	48% - 48%#
Canada	43,247	21,051 - 26,564	51,958	25,292 - 31,915	49% - 61%
United states	53,143	24,283 - 40,112	53,042	24,283 - 40,112	46% - 75%
Norway	65,461	28,057 - 60,862	100,819	43,211 - 93,736	43% - 93%
Low/middle income*	1,045	16 - 537	Not available		1% - 51%
Middle/high income*	12,746	2,307 - 9,028			18% - 71%

* We have assumed Gross National Income per capita to be the same as PPP adjusted GDP. These values relate to the income cut-offs for low to middle income and middle to high income countries as defined by the World Bank.

+ Reflects range of values obtained when using elasticity estimates of 1.0, 1.5, 2.0 and 2.5 for GDP less than $10,725 (2005 PPP USD) and 0.7 for GDP greater than $10,725 (2005 PPP USD).

For the UK, the World Bank ratio of PPP conversion factor to market exchange rate did not correspond to the ratio of reported actual GDP to reported PPP-adjusted GDP. The threshold

as a % GDP value for the UK, therefore, depends on whether PPP-adjusted or actual data are used (51% and 48% respectively).

Appendix: All country values

The table below presents the PPP-adjusted and non-adjusted range of threshold values for each country for which PPP-adjusted GDP was reported in the World Bank database. In some cases data was not available to remove the PPP-adjustment and only PPP-adjusted threshold values are reported.

Country	Cost-effectiveness threshold range (USD, PPP adjusted)	Cost-effectiveness threshold range (actual USD)
Afghanistan	56 - 1,023	19 - 349
Albania	1,563 - 5,816	702 - 2,612
Algeria	2,514 - 9,300	1,012 - 3,743
Angola	807 - 3,875	603 - 2,897
Antigua and Barbuda	6,250 - 12,750	3,965 - 8,090
Armenia	858 - 3,997	387 - 1,801
Australia	21,153 - 26,938	32,771 - 41,732
Austria	21,355 - 27,684	23,727 - 30,759
Azerbaijan	4,172 - 11,085	1,901 - 5,051
Bahrain	21,245 - 27,277	11,962 - 15,358
Bangladesh	93 - 1,315	30 - 427
Belarus	4,407 - 11,297	1,895 - 4,857
Belgium	20,060 - 23,111	22,570 - 26,003
Belize	1,012 - 4,340	584 - 2,503
Benin	46 - 921	20 - 414
Bhutan	835 - 3,943	267 - 1,258
Bolivia	534 - 3,151	250 - 1,474
Bosnia and Herzegovina	1,318 - 4,952	644 - 2,421
Botswana	3,490 - 10,419	1,621 - 4,839
Brazil	3,210 - 10,122	2,393 - 7,544

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	**(actual USD)**
Brunei Darussalam	29,901 - 73,137	16,065 - 39,294
Bulgaria	3,609 - 10,541	1,720 - 5,025
Burkina Faso	38 - 840	17 - 379
Burundi	8 - 396	3 - 137
Cabo Verde	584 - 3,297	343 - 1,935
Cambodia	131 - 1,564	44 - 518
Cameroon	104 - 1,394	49 - 654
Canada	21,051 - 26,564	25,292 - 31,915
Central African Republic	5 - 310	3 - 171
Chad	61 - 1,070	31 - 540
Chile	6,819 - 13,141	4,896 - 9,436
China	2,013 - 7,957	1,151 - 4,550
Colombia	2,174 - 8,754	1,370 - 5,518
Comoros	35 - 801	19 - 452
Congo, Dem. Rep.	8 - 384	5 - 230
Congo, Rep.	489 - 3,016	264 - 1,628
Costa Rica	2,733 - 9,574	2,006 - 7,027
Cote d'Ivoire	129 - 1,548	61 - 737
Croatia	6,206 - 12,720	3,953 - 8,101
Cyprus	12,318 - 16,130	11,020 - 14,430
Czech Republic	10,620 - 15,322	7,325 - 10,569
Denmark	20,888 - 25,974	28,767 - 35,771
Djibouti	128 - 1,541	71 - 857
Dominica	1,429 - 5,205	991 - 3,611
Dominican Republic	1,943 - 7,618	937 - 3,675
Ecuador	1,557 - 5,788	858 - 3,191

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Egypt, Arab Rep.	1,745 - 6,669	522 - 1,993
El Salvador	856 - 3,991	422 - 1,967
Equatorial Guinea	16,150 - 17,717	9,843 - 10,798
Eritrea	20 - 615	9 - 280
Estonia	8,912 - 14,418	6,574 - 10,636
Ethiopia	26 - 696	10 - 255
Fiji	897 - 4,086	507 - 2,307
Finland	19,334 - 20,781	23,867 - 25,653
France	18,861 - 19,347	21,168 - 21,713
Gabon	5,268 - 12,018	3,164 - 7,218
Gambia, The	39 - 857	12 - 252
Georgia	729 - 3,683	366 - 1,850
Germany	21,080 - 26,668	21,933 - 27,747
Ghana	224 - 2,043	104 - 951
Greece	9,345 - 14,658	7,982 - 12,520
Grenada	1,878 - 7,302	1,272 - 4,948
Guatemala	756 - 3,750	360 - 1,788
Guinea	22 - 645	9 - 269
Guinea-Bissau	22 - 639	9 - 256
Guyana	610 - 3,368	348 - 1,924
Haiti	41 - 875	20 - 421
Honduras	299 - 2,360	149 - 1,177
Hong Kong SAR, China	24,302 - 40,202	17,409 - 28,801
Hungary	7,434 - 13,540	4,268 - 7,773
Iceland	19,942 - 22,720	22,567 - 25,712
India	416 - 2,781	115 - 770

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Indonesia	1,298 - 4,914	472 - 1,786
Iran, Islamic Rep.	3,450 - 10,378	1,054 - 3,171
Iraq	3,276 - 10,194	1,504 - 4,679
Ireland	21,071 - 26,634	23,063 - 29,153
Israel	15,243 - 17,366	16,821 - 19,163
Italy	16,712 - 17,928	16,867 - 18,094
Jamaica	1,122 - 4,570	668 - 2,719
Japan	18,651 - 18,731	19,769 - 19,854
Jordan	1,971 - 7,757	872 - 3,432
Kazakhstan	7,648 - 13,675	4,485 - 8,018
Kenya	73 - 1,164	32 - 519
Kiribati	49 - 954	43 - 848
Korea, Rep.	15,598 - 17,505	12,227 - 13,722
Kosovo	1,085 - 4,493	473 - 1,961
Kyrgyz Republic	147 - 1,651	58 - 649
Lao PDR	329 - 2,474	113 - 852
Latvia	7,532 - 13,602	5,133 - 9,270
Lebanon	4,187 - 11,098	2,420 - 6,416
Lesotho	95 - 1,329	41 - 581
Liberia	11 - 451	6 - 234
Libya	6,503 - 12,927	3,697 - 7,349
Lithuania	9,175 - 14,565	5,598 - 8,886
Luxembourg	35,195 - 117,072	43,092 - 143,342
Macao SAR, China	48,116 - 288,671	30,832 - 184,977
Macedonia, FYR	1,978 - 7,791	824 - 3,246
Madagascar	28 - 717	9 - 235

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Malawi	9 - 401	3 - 116
Malaysia	7,709 - 13,712	3,481 - 6,192
Maldives	1,929 - 7,550	1,103 - 4,318
Mali	38 - 844	17 - 368
Malta	12,965 - 16,419	10,138 - 12,838
Marshall Islands	196 - 1,908	182 - 1,774
Mauritania	131 - 1,564	46 - 550
Mauritius	4,202 - 11,112	2,248 - 5,945
Mexico	3,850 - 10,780	2,410 - 6,749
Micronesia, Fed. Sts.	180 - 1,829	162 - 1,646
Moldova	310 - 2,400	148 - 1,151
Mongolia	1,264 - 4,849	543 - 2,085
Montenegro	2,912 - 9,786	1,464 - 4,921
Morocco	736 - 3,702	316 - 1,590
Mozambique	16 - 537	8 - 294
Namibia	1,332 - 4,979	791 - 2,958
Nepal	72 - 1,154	22 - 357
Netherlands	21,104 - 26,757	23,153 - 29,354
New Zealand	17,226 - 18,117	20,555 - 21,619
Nicaragua	297 - 2,350	118 - 937
Niger	12 - 469	5 - 213
Nigeria	446 - 2,880	239 - 1,545
Norway	28,057 - 60,862	43,211 - 93,736
Oman	21,322 - 27,562	
Pakistan	314 - 2,416	87 - 669
Palau	3,235 - 10,149	2,531 - 7,940

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Panama	5,352 - 12,083	3,042 - 6,869
Papua New Guinea	92 - 1,305	75 - 1,073
Paraguay	919 - 4,135	484 - 2,179
Peru	1,969 - 7,747	1,114 - 4,383
Philippines	606 - 3,358	256 - 1,421
Poland	7,694 - 13,703	4,440 - 7,908
Portugal	9,527 - 14,756	7,738 - 11,985
Puerto Rico	17,145 - 18,088	14,075 - 14,849
Qatar	45,558 - 246,565	31,105 - 168,345
Romania	4,932 - 11,746	2,467 - 5,875
Russian Federation	8,263 - 14,046	5,007 - 8,511
Rwanda	30 - 746	13 - 323
Samoa	363 - 2,598	265 - 1,897
Sao Tome and Principe	125 - 1,527	68 - 827
Saudi Arabia	24,484 - 41,080	11,799 - 19,797
Senegal	73 - 1,166	34 - 544
Serbia	2,175 - 8,760	1,061 - 4,275
Seychelles	8,310 - 14,074	5,470 - 9,265
Sierra Leone	53 - 990	23 - 435
Singapore	31,889 - 88,068	22,342 - 61,701
Slovak Republic	9,686 - 14,841	6,561 - 10,053
Slovenia	11,374 - 15,690	9,135 - 12,603
Solomon Islands	61 - 1,063	57 - 1,004
South Africa	2,221 - 8,909	1,175 - 4,714
South Sudan	77 - 1,198	40 - 617
Spain	14,638 - 17,124	13,277 - 15,531

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Sri Lanka	1,346 - 5,005	453 - 1,686
St. Kitts and Nevis	6,222 - 12,731	4,110 - 8,409
St. Lucia	1,584 - 5,914	1,107 - 4,133
St. Vincent and the Grenadines	1,615 - 6,058	998 - 3,746
Sudan	162 - 1,734	84 - 901
Suriname	3,740 - 10,672	2,286 - 6,525
Swaziland	634 - 3,436	288 - 1,559
Sweden	21,148 - 26,917	28,306 - 36,028
Switzerland	24,450 - 40,914	36,661 - 61,348
Tajikistan	90 - 1,291	37 - 533
Tanzania	45 - 912	18 - 357
Thailand	2,941 - 9,820	1,181 - 3,943
Timor-Leste	71 - 1,153	
Togo	27 - 715	13 - 327
Tonga	399 - 2,726	333 - 2,275
Trinidad and Tobago	13,159 - 16,503	7,941 - 9,959
Tunisia	1,747 - 6,680	678 - 2,592
Turkey	5,114 - 11,895	2,950 - 6,861
Turkmenistan	2,784 - 9,635	1,588 - 5,495
Tuvalu	188 - 1,870	200 - 1,991
Uganda	28 - 725	11 - 293
Ukraine	1,097 - 4,518	487 - 2,005
United Kingdom	18,609 - 18,609	20,223 - 20,223
United States	24,283 - 40,112	24,283 - 40,112
Uruguay	5,450 - 12,160	4,548 - 10,147
Uzbekistan	379 - 2,656	138 - 965

Country	Cost-effectiveness threshold range (USD, PPP adjusted)	(actual USD)
Vanuatu	127 - 1,538	139 - 1,685
Venezuela, RB	4,701 - 11,553	3,724 - 9,151
Vietnam	398 - 2,721	144 - 982
Yemen, Rep.	223 - 2,035	83 - 757
Zambia	144 - 1,635	68 - 768
Zimbabwe	41 - 874	21 - 455